

AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings in this application.

Listing of Claims

1-37. (Canceled)

38. (Previously Presented) A virion comprising a tissue-specific replication-conditional adenoviral vector comprising:

(a) a heterologous tissue-specific transcriptional regulatory sequence operably linked to the coding region of a gene that is essential for replication of said vector, wherein said coding region is an E1a, E1b, E2, or E4 coding region; and

(b) at least one additional coding sequence encoding a heterologous gene product, wherein said additional coding sequence is operably linked to said heterologous tissue-specific transcriptional regulatory sequence.

39. (Original) The virion of claim 38, wherein said tissue-specific transcriptional regulatory sequence is a promoter or an enhancer.

40. (Original) The virion of claim 39, where said promoter is selected from the group consisting of an MUC1/DF3 promoter, an alpha-fetoprotein promoter, an erb-B2 promoter, a surfactant promoter, a thymidine kinase promoter, a p21 promoter, and a cyclin promoter.

41. (Original) The virion of claim 39, wherein said enhancer is selected from the group consisting of DF3, a breast cancer-specific enhancer, viral enhancers, and steroid receptor enhancers.

42. (Original) The virion of claim 38, wherein said additional coding sequence is selected from the group consisting of a thymidine kinase coding sequence, a cytosine deaminase coding sequence, and a purine nucleoside phosphorylase coding sequence.

43. (Original) An isolated cell comprising the virion of claim 38.

44. (Currently Amended) An isolated cell comprising the virion of claim 38, wherein said transcriptional regulatory sequence functions in said cell so that replication of said virion and expression of said additional coding sequence occurs in said cell. ~~An isolated cell comprising the virion of claim 38, wherein said transcriptional regulatory sequence functions in said cell so that replication said cell.~~

45. (Original) The cell of claim 43, wherein said cell is a tumor cell or an abnormally proliferating cell.

46. (Original) The cell of claim 45, wherein said additional coding sequence provides a gene product that provides anti-tumor activity in said cell.

47. (Original) The cell of claim 45, wherein said tumor cell is selected from the group consisting of a hepatoma cell, and lung carcinoma cell.

48. (Original) A method of producing the virion of claim 38, comprising culturing a cell infected with said virion and recovering said virion from said cell.

49. (Original) The virion of claim 38, wherein said additional coding sequence expresses a gene product that can reduce or eliminate virion replication.

50. (Original) The virion of claim 49, wherein said gene product is selected from the group consisting of cytosine deaminase, thymidine kinase, and purine nucleoside phosphorylase.

51. (Previously Presented) A virion comprising a tissue-specific replication-conditional adenoviral vector comprising:

(a) a heterologous tissue-specific transcriptional regulatory sequence operably linked to the coding region of the adenovirus E1a gene that is essential for replication of said vector; and

(b) at least one additional coding sequence encoding a heterologous gene product, wherein said additional coding sequence is operably linked to a second transcriptional regulatory sequence that is activated by the E1a gene product.

52. (Original) The virion of claim 51, wherein said at least one additional coding sequence replaces a coding

sequence of a gene in said vector, which gene is not essential for vector replication, such that said at least one additional coding sequence is operably linked to and transcribed from said second transcriptional regulatory sequence.

53. (Original) The virion of claim 51, wherein at least one of said transcriptional regulatory sequences is a promoter or an enhancer.

54. (Original) The virion of claim 53, where said promoter is selected from the group consisting of an MUC1/DF3 promoter, an alpha-fetoprotein promoter, an erb-B2 promoter, a surfactant promoter, a thymidine kinase promoter, a p21 promoter, and a cyclin promoter.

55. (Original) The virion of claim 53, wherein said enhancer is selected from the group consisting of DF3, a breast cancer-specific enhancer, a viral enhancer, and a steroid receptor enhancer.

56. (Original) The virion of claim 51, wherein said additional coding sequence is selected from the group consisting of a thymidine kinase coding sequence, a cytosine deaminase coding sequence, and a purine nucleoside phosphorylase coding sequence.

57. (Original) The virion of claim 51, wherein said at least one additional coding sequence encodes a gene product that can reduce or eliminate replication of said vector.

58. (Original) The virion of claim 57, wherein said gene product is selected from the group consisting of cytosine deaminase, thymidine kinase, and purine nucleoside phosphorylase.

59. (Original) An isolated cell comprising the virion of claim 51.

60. (Original) An isolated cell comprising the virion of claim 51, wherein said transcriptional regulatory sequence operably linked to the coding region of the adenovirus Ela gene functions in said cell so that replication of said virion and expression of said additional coding sequence occurs in said cell.

61. (Original) The cell of claim 59, wherein said cell is a tumor cell or an abnormally proliferating cell.

62. (Original) The cell of claim 61, wherein said at least one additional coding sequence encodes a gene product that provides anti-tumor activity in said cell.

63. (Original) The cell of claim 61, wherein said tumor cell is selected from the group consisting of a hepatoma cell and lung carcinoma cell.

64. (Previously Presented) A method of producing a virion according to claim 51, comprising culturing a cell infected with said virion and recovering virions produced by said cell.

65. (Original) The virion of claim 38, wherein said transcriptional regulatory sequence is a tumor-specific regulatory sequence.

66. (Original) The virion of claim 65, wherein said tumor-specific regulatory sequence is a tumor-specific promoter.

67. (Original) The virion of claim 38, wherein said transcriptional regulatory sequence is an alpha-fetoprotein promoter.

68. (Original) The virion of claim 38, wherein said coding region is the E1a coding region.

69. (Original) The virion of claim 38, wherein said coding region is the E1b coding region.

70. (Original) The virion of claim 38, wherein said coding region is an E2 coding region.

71. (Original) The virion of claim 70, wherein said coding region is the E2a coding region.

72. (Original) The virion of claim 38, wherein said coding region is the E4 coding region.

73. (Original) The virion of claim 38, wherein said additional coding sequence is a thymidine kinase coding sequence.

74. (Original) The cell of claim 43, wherein said transcriptional regulatory sequence is a tumor-specific regulatory sequence.

75. (Original) The cell of claim 74, wherein said tumor-specific regulatory sequence is a tumor-specific promoter.

76. (Original) The cell of claim 43, wherein said transcriptional regulatory sequence is an alpha-fetoprotein promoter.

77. (Original) The cell of claim 43, wherein said coding region is the E1a coding region.

78. (Original) The cell of claim 43, wherein said coding region is the E1b coding region.

79. (Original) The cell of claim 43, wherein said coding region is an E2 coding region.

80. (Original) The cell of claim 79, wherein said coding region is the E2a coding region.

81. (Original) The cell of claim 43, wherein said coding region is the E4 coding region.

82. (Original) The cell of claim 43, wherein said additional coding sequence is a thymidine kinase coding sequence.

83. (Original) The virion of claim 51, wherein said transcriptional regulatory sequence operably linked to the coding region of the adenovirus Ela gene is a tumor-specific regulatory sequence.

84. (Previously Presented) The virion of claim 83, wherein said tumor-specific regulatory sequence operably linked to the coding region of the adenovirus Ela gene is a tumor-specific promoter.

85. (Original) The virion of claim 51, wherein said transcriptional regulatory sequence operably linked to the coding region of the adenovirus Ela gene is an alpha-fetoprotein promoter.

86. (Previously Presented) The virion of claim 51, wherein said at least one additional coding sequence replaces a coding sequence of the adenovirus E3 gene in said vector, such that said at least one additional coding sequence is operably linked to and transcribed from said second transcriptional regulatory sequence.

87. (Original) The virion of claim 86, wherein said second transcriptional regulatory sequence is an adenovirus E3 promoter.

88. (Original) The virion of claim 51, wherein said additional coding sequence is a thymidine kinase coding sequence.

89. (Original) The virion of claim 87, wherein said additional coding sequence is a thymidine kinase coding sequence.

90. (Previously Presented) The cell of claim 59, wherein said transcriptional regulatory sequence operably linked to the coding region of the adenovirus Ela gene is a tumor-specific regulatory sequence.

91. (Original) The cell of claim 90, wherein said tumor-specific regulatory sequence operably linked to the coding region of the adenovirus Ela gene is a tumor-specific promoter.

92. (Original) The cell of claim 59, wherein said transcriptional regulatory sequence operably linked to the coding region of the adenovirus Ela gene is an alpha-fetoprotein promoter.

93. (Original) The cell of claim 59, wherein said at least one additional coding sequence replaces a coding sequence of the adenovirus E3 gene in said vector, such that said at least one additional coding sequence is operably linked to and transcribed from said second transcriptional regulatory sequence.

94. (Original) The cell of claim 93, wherein said second transcriptional regulatory sequence is an adenovirus E3 promoter.

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95. (Original) The cell of claim 59, wherein said additional coding sequence is a thymidine kinase coding sequence.

96. (Original) The cell of claim 94, wherein said additional coding sequence is a thymidine kinase coding sequence.